STATUS OF THE CLAIMS

Claims 1-6,12-16, and 21-22 are rejected under 35 U.S.C., 112, first paragraph.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph.

Claims 1-29 are rejection under 35 U.S.C. 102(e) or, alternatively under 103(a).

Claims 1-5, 7-8 and 10-16 are rejected under 35 U.S.C. 103(a).

Claim 17 is objected to.

AMENDMENTS

Basis for the present amendments can be found in the original claims and throughout the specification as originally filed. No new matter has been added, nor has the scope of the claims been broadened by these amendments.

REMARKS

Applicants appreciate the Examiner's careful review of the Specification. Amendments have been made to the Specification in order to fill in the serial numbers missing throughout the specification.

Restriction Requirement

In a telephone conversation on January 30, 2003 the Examiner stated that the claims of this application recite 4 separate classes of invention and required that the Applicant elect one of these classes for prosecution. Applicants provisionally elected the invention of group II, claim 2, 16-17 and generic claims 1, 3-8, 10-15, 18 and 21-22 reading on claim 2 compounds. Applicants hereby confirm this election and reserve the right to either rejoin the non-elected (withdrawn) claims according to the direction of MPEP 821.04 or to pursue the non-elected invention of Groups I, III and IV in a divisional or continuing application.

Rejections under U.S.C 112

With the exception of acylated amino functionalities, the Examiner rejected claims 1-6 and 12-16 for lack of enablement contending that the term "prodrug" can cover from a "a single acylation to a convoluted preparation such as prolong release targeted conjugate, etc." The Examiner also alleges that the term "wherein two . . . are joined to form a fused ring" as identified on pages 16-17 is indefinite and explains that it is indefinite because one skilled in the art would be unable to decide whether starting material is available to make the compound. Applicants respectfully traverse.

Based on what is common knowledge in chemistry, one of skill in the art could easily identify and prepare prodrugs of the compounds of the present invention, especially the presently amended scope of compounds, without undue experimentation. See, for example:

a) Design of Prodrugs, edited by H. Bundgaard, (Elsevier, 1985) and Methods in Enzymology, Vol.42, p. 309-396, edited by K. Widder, *et al.* (Acamedic Press, 1985);

b) A Textbook of Drug Design and Development, edited by Krosgaard-Larsen and H. Bundgaard, Chapter 5, "Design and Application of Prodrugs," by H. Bundgaard, pp. 113-191 (1991); and

c) H. Bundgaard, Advanced Drug Delivery Reviews, 8, 1-38 (1992).

The references cited above provide ample examples of prodrugs known in the art, from simple acylations to prolonged release formulations, and the means for obtaining such compounds. Accordingly, Applicants request withdrawal of the enablement rejection based on the term "prodrug".

With respect to the rejection based on the term "wherein two. . . are joined to form a fused ring", Applicants believe that ample information is given in the Specification to enable one of skill in the art to identify appropriate starting materials. In particular, the synthetic schemes I-III on pages 21-25 of the Specification provide a detailed description of the preparation of the compounds of the present invention, making it explicit which starting materials must be used to achieve the corresponding desired products – whether or not the compounds contain fused rings. Accordingly, Applicants request withdrawal of the indefiniteness rejection over use of the term "wherein two. . . are joined to form a fused ring".

The Examiner has rejected claims 21-22 under 35 U.S.C., first paragraph contending that the specification does not reasonably provide enablement for the scope of conditions associated with melanocortin receptors, noting that a compound cannot simultaneously act as BOTH and agonist and antagonist. In response, Applicants have amended the claims to specify the specific conditions that are treatable by their compounds, i.e. melanocortin receptor associated conditions that are treated by agonizing the receptors. Accordingly, Applicants believe the enablement rejection is now moot.

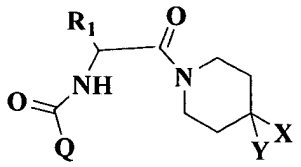
The Examiner also rejected Claim 18 for being indefinite as the Examiner contends that a pharmaceutical without dosage limitations may be ineffective or toxic. In response, Applicants have amended Claim 18 to incorporate the Examiner's suggested limitation of a "therapeutically effective amount".

Rejections under 35 U.S.C. 102(e)/103(a)

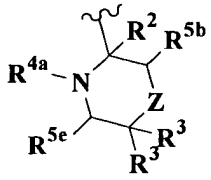
The Examiner has rejected Claims 1-2, 4-5, 10, 14, 18 and 21-22 under 35 U.S.C. 102(e), or, in the alternative U.S.C. 103(a), as being anticipated or rendered obvious by US 6,458,790

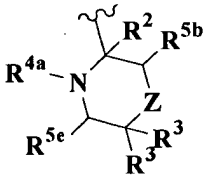
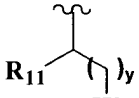
("Palucki"). The Examiner contended that every element of the Applicants claims where W is piperazinyl optionally substituted or optionally fused, were anticipated by Palucki. In the alternative, the Examiner rejected the claims contending that Palucki disclosed all the elements of the claims "except a species wherein one of R_8 or R_9 being cycloalkyl and heteroarylalkyl while W is piperazine" and that such modification was obvious. Applicants respectfully traverse.

Palucki's claimed compounds are represented by the following generic structure:



where Z is O, S or NR^{4b}; and

Q is  . Accordingly, for Applicants compounds to read on Palucki's generic structure,

 must correspond to Applicants' group  , and there must exist in Applicants claimed generic structure the possibility that R_{11} may be taken together with W to form the Palucki heterocyclo "Q" group. However, Applicants' claimed compounds do not include this possibility, and thus are not described or anticipated by Palucki's claimed generic structure. Since this is true, regardless of whether R_8 or R_9 are cycloalkyl and heteroarylalkyl groups or not, Applicants assert that the rejection for lack of obviousness is also overcome. Accordingly, Applicants request withdrawal of the rejections under 35 U.S.C.§§ 102(e) and 103(a) over Palucki.

Rejections under 103(a)

The Examiner further rejected claims 1-5, 7-8, and 10-16 under 35 U.S.C. §103(a) over US 5,622,973 ("Morriello") in view of US 6,303,620 ("Hansen") contending that Morriello disclosed structurally similar compounds and that the variation in position isomerism as taught by Hansen would have made reasonable the expectation that such isomers would have similar art recognized activity and that Applicants claimed compounds, as positional isomers of Morriello, are obvious. Applicants respectfully traverse.

Both Morriello and Hansen teach compounds having growth hormone secretage ("GSH") activity useful in the treatment of growth-associated disorders. In contrast, Applicants' compounds target melanocortin receptors thereby operating via a very different mechanism and resulting in a

very different use (treatment of inflammatory or immune disease, cardiovascular disease or neurodegenerative disease) as compared to a GSH compound. At most, the teaching of Hansen in combination with Morriello may be helpful in obtaining compounds that have GSH activity, but there is no teaching that would lead one of skill in the art to design compounds that have melanocortin receptor activity. Accordingly, it would not be obvious to one of skill in the art to use Hansen's teaching to vary the positional isomerism of Moriello's GSH compounds to discover Applicants claimed compounds. It is requested that the Examiner's rejection for obviousness over claims 1-5, 7-8, and 10-16 be withdrawn.

Objections

The Examiner objected to claim 17 as being dependent upon a rejected base claim 1. Applicants believe that amended claim 1 is now allowable and believe this objection is now moot.

Summary

The Applicants believe the claims, as amended, are now in condition for allowance. The Examiner is invited to contact the undersigned by telephone, at the number listed below, if it is believed that a telephonic communication would facilitate the prosecution of this application.

FEES

No fees should be due. However, if it is determined that a fee is due, please charge same to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

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Date: September 5, 2003